BIOC 482/552: Structural Biology

Credits: 3

Prerequisites: Concurrent or prior biochemistry; and freshman physics or equivalent

Date/Time/Place: Spring 2022, 10:00-10:50 AM, MWF, Keck Hall 105 MW and GEO 130 Fridays

Instructors: George N. Phillips (georgep@rice.edu), Ed Nikonowicz (edn@rice.edu)
TA/Homework: Mitch Miller (mitchm@rice.edu) Office hours by appointment.

Textbook/Readings: Lattman and Loll, Protein crystallography: A concise guide. 2008, Johns Hopkins Press (Kindle or Amazon), IUCr On-line dictionary of crystallography (free access),

Course Description: Structural biology plays an important role in defining atomic structures of biomolecules and understanding relationships between structure, dynamics and function. This course will give an introduction to techniques of determining bimolecular structures, X-ray crystallography, NMR, and cryoelectron microscopy and discuss striking examples of the power of structural biology including biomedical examples. It will provide knowledge of techniques used to obtain detailed structural and dynamic information about biological macromolecules. Designed for advanced undergraduates and beginning graduate students in the biological or physical sciences. Students will present short vignettes on interesting structural results and will design and print 3-D models on a color printer as a part of their presentation. There will be two short in-class exams, homework and a presentation with 3-D printer support, but no final exam. BIOC 553 students (graduate students) will be required to give two presentations. Mondays and Wednesdays will be structural biology techniques and examples in biomedicine, Fridays will be practical homework/discussion sections.

Course Objectives and expected learning outcomes:

- To introduce the fundamental theory and the practice of X-ray crystallography and NMR in modern structural biology and biomedicine
- To evaluate the research articles from the primary literature to understand and analyze advanced topics in X-ray crystallography, with an emphasis on fundamental principles, research methodologies, and emerging research topics.
- To improve scientific communication skills through explaining conclusions and methodology to the group and fielding questions.

Grading: Course grade based equally on three components. Homeworks, Exams, Presentation(s).
The presentation will include production of a 3-D printed model of a macromolecule and a 20 minute talk.

Rice Honor Code: Students are required to use proper citations and follow other practices outlined in the Rice Honor Code information on Academic Fraud and Acknowledgement of Sources: http://honor.rice.edu/honor-system-handbook/

Accommodations for students with disabilities: Any student with a documented disability needing academic adjustments or accommodations is requested to speak with the instructor during the first two weeks of class. All discussions will remain confidential. Students with disabilities also should contact Disability Support Services in Allen Center.

Teaching will be offered in person as soon as allowed and recorded for off-line/remote viewing.

Topics to be covered:

Overview of imaging and role of structural methods in modern science
Symmetry (point groups, 2D, 3D, icosahedra: Crystallization of proteins
Diffraction from cyrstalline objects, Reciprocal space
Electron density equation, Phase problem, Patterson function, Heavy atom/direct methods, isomorphous replacement
Molecular replacement, Non-crystallographic averaging, refinement, Laue methods, synchrotrons, phasing
X-ray fiber diffraction, solution scattering
NMR methods of structure determination
High resolution electron microscopy
Molecular Dynamics Simulations
Analysis of electrostatics of proteins
Structure-based drug design

Student and others' presentations on interesting biological systems and 3-d printing of molecules

Preliminary Schedule

Week 1

Jan 10	Introduction to class and requirements
	Brief review of chemical structure of proteins and nucleic acids
Jan 12	Brief overview of crystallography
Jan 14	HW1- PYMOL intro (Geo Lab)

Week 2

Jan 17	Review of complex numbers and operators needed in the class
	Scattering and illustration of how diffraction is the sum of waves
	Comparison of imaging methods in biology.
Jan 19	Lattices, unit cells (Geo Lab)
	Symmetry
	Space groups
	Miller indices
Jan 21	HW2 – scattering and symmetry

Week 3

Jan 24	Diffraction from arbitrary objects, slits and from lattices
Jan 26	Reciprocal Space
	Bragg's Law
	X-ray sources
	Crystal mounting
Jan 28	HW3 1-d transform exercise, X-RayView exercises,

Week 4

Jan 31	Electron density equation
	The Phase Problem
Feb 2	ED as sum of waves, direct methods
Feb 4	HW3 1-d transform exercise

Week 5

Feb 7	Phase problem continued, molecular replacement
	Difference maps

	Refinement and R-free, Cross-validation
	Specialized Maps
Feb 9	PDB validation and deposition
Feb 11	Field trip to crystallography lab

Week 6

Feb 14	
Feb 16	Diffraction from helices
	Discovery of the double helix and other helical objects
	Diffraction from membranes, solutions and examples
Feb 18	Exam Review

Week 7

Feb 21	Crystallography Exam
Feb 23	Basics of NMR
Feb 27	One- and Two-dimensional NMR Experiments

Week 8

Feb 28	Two-dimensional NMR Experiments continued
Mar 2	Structural Constraints from NMR, Integration with MD Simulations
Mar 4	NMR instrument operation

Week 9

Mar 7	The phenomenon of chemical exchange
Mar 9	Relaxation-dispersion and measuring microsecond timescale motions
Mar 11	Additional types of structure constraints:
	Residual dipolar couplings
	Chemical shift tensors
	NMR Problem Set due

March 12-20 Spring Break

Week 10

Mar 21	Dealing with the molecular size problem
	Transverse Relaxation Optimized Spectroscopy
	Random fractional deuteration
Mar 23	Application of NMR to *very* big protein and RNA complexes
Mar 25	NMR exam

Week 11

Mar 28	Electron microscopy**,** Single particle Cryo-EM
Mar 30	Molecular Dynamics Simulations
Apr 1	NAMD Exercise, finish model to be printed

Week 12

Apr 4	Protein folding – Anfinsen dogma
	Measurement of folding/unfolding
	Anton machine
Apr 6	CASP, Homology Modeling, Alpha-fold
	BLAST
Apr 8	BLAST/homology exercise,

Week 13

Apr 11	Student presentations
Apr 13	Student presentations
Apr 15	Student presentations

Week 14

Apr 18	Student presentations
Apr 20	Student presentations